

to apply a voltage drop across two parallel discs as shown in **FIG. 18**. This method is simple but unless the discs are very large the maximum drift distance that can be used is very limited due to the non-linearity produced by fringing fields. To increase the drift distance yet maintain adequate resolution at the expense of field linearity a radius of curvature has been added to the electrode yielding focusing properties to increase the drift cell sensitivity.

Radius of Curvature Electrode

[0103] **FIG. 19** shows the equipotential lines formed between an electrode with a 6" radius of curvature and a grounded flat plate. Note that the region of linearity may be lengthened by using a vacuum can of insulating material, e.g. glass or plastic in which case the penetrating fields are eliminated. This embodiment of the present invention is easy to manufacture and assemble, and is very robust. The drift cell interior is accessible by removing the top view port for cleaning resulting in short down times between experiments. The device also provides moderate resolution (20-40) and high sensitivity (10 femtomoles of loaded sample).

Field Correcting Ring Electrode

[0104] **FIG. 20** illustrates the equipotential lines in an embodiment of the present invention having a field correcting ring in addition to flat disc electrode. A device so configured can be adjusted to produce an interior electric field ranging from linear to highly non-linear and all combinations between.

Flat Disc with Second Movable Cylindrical Electrode

[0105] **FIG. 21** illustrates the equipotential lines in another embodiment having a flat electrode and a second movable electrode. Such a device can be adjusted to produce an interior electric field ranging from linear to highly non-linear and a continuous range of combinations in between.

RF Focusing Interface

[0106] The embodiment of the present invention as depicted in **FIG. 16** is limited to a drift/buffer gas pressure of 1-50 Torr due to a single stage of pumping on the ion detector and mass spectrometer. A higher operating buffer gas pressure allows for a higher electrode voltage and subsequent higher resolution. To maintain a collision free vacuum in the analyzer chamber at higher drift cell pressures requires either the use of larger vacuum pumps or an additional stage of differential pumping. But a standard interface operating at ca. 1 Torr would compromise the sensitivity of the apparatus due to excessive ion losses. Several reported attempts have been made to increase the ion transmission in an interface region. Smith et al. implemented an ion funnel (PCT WO 97/49111), consisting of a series of decreasing diameter ring electrodes to which an alternating RF voltage and linear DC voltage is applied. Krutchinsky et al. used a segmented RF only quadrupole (Proceedings of the 43rd ASMS Conference, 1995, 126). Both could increase the ion transmission significantly. It is a further object of the present invention to provide a simple, yet highly efficient ion interface to transport ions through an intermediate region between a high background pressure device and a high vacuum device. Without compromising

the small scale dimensions of the apparatus an alternative embodiment comprising a radio frequency focusing interface. In this embodiment, ions exiting aperture 12 (see **FIG. 16**) encounter a combination of a RF electric field and a DC electric field in the presence of buffer gas collisions. The resulting ion trajectories are shown in **FIG. 22**, illustrating the superb focusing characteristics of this device.

Microchannel Plate Aperture

[0107] **FIG. 23** shows a schematic of an alternative embodiment of one section of the present invention comprising the aperture plate by which ions are sampled. The mobility chamber 5 at high pressure is separated from the analyzer chamber 6 at vacuum by a multi-capillary interface, e.g. a microchannel plate 1. High ion transmission can be achieved by reverse biasing a semi-conductive capillary in the presence of gas flow and a temperature gradient as described in U.S. Pat. No. 5,736,740 to Franzen. The preferred embodiment of the present invention utilizes a bundle of capillaries acting as a pressure stop and ion interface to reduce the vacuum pump requirements. The optimum diameter to length ratio will depend on the required pressure drop as well as on the absolute pressure. The diameter of the microchannel interface can be much larger than a single aperture thereby transmitting ions that diffuse in the radial direction in the drift chamber that would otherwise be lost.

Mobility/MS/MS

[0108] A further alternate embodiment of the present invention comprises pre-selecting parent ions by their mobility for fragmentation. The form of fragmentation includes in part, methods known in the art such as collision-induced dissociation (CID), surface-induced dissociation (SID), electron impact or photo-induced dissociation with the preferred method of dissociation being SID. In **FIG. 16**, the SID surface 18 is located between lens system 4 and time-of-flight source 13 and preferably is comprised of a rotatable fine mesh grid. The advantage of the present invention embodiment is the simultaneous detection of parent and fragment ions: fragment ions will appear at the same mobility time as the parent ions without scanning the entire mass range at a specific mobility drift time. To eliminate any energy differences between the parent and fragment ions that occur during the dissociation process a RF focusing quadrupole onto which a linear electric field in superimposed is located behind the (SID) grid. All ions are cooled by collisions in the RF quadrupole and therefore arrive at the time-of-flight source simultaneously. Because higher energy collisions in CID result in a greater degree of fragmentation, the collision energy may be increased by using an electric field to accelerate the ions within the expanding gas flow during transmission from the ion mobility drift cell to the mass spectrometer.

Performance

[0109] One of the many applications of the apparatus is in the field of proteomics, specifically protein mixture analysis. Current analytical techniques are time consuming and labor intensive but a gas phase separation method such as ion mobility spectrometry is more congruous with mass analysis so by combining the separation step and the mass analysis into a single instrument as in the present invention the throughput of the system is greatly increased. Also, the